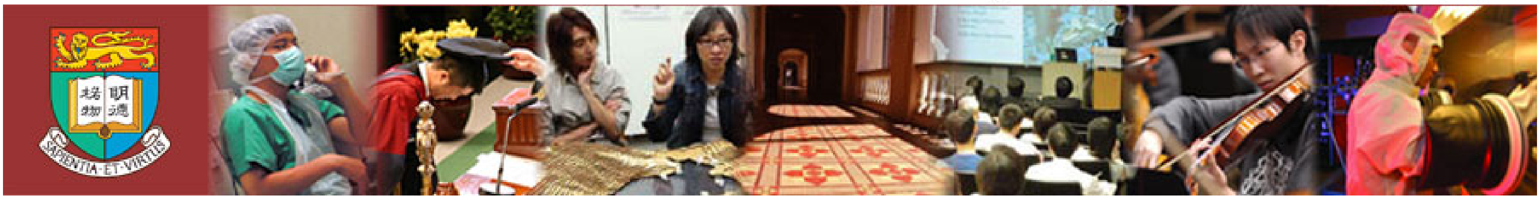

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F_4H_5: a novel substance for the removal of silicone oil from intraocular lenses

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ABSTRACT

Aim Adherent silicone oil on intraocular lenses (IOLs) following retinal detachment surgery induces large and irregular refractive errors and multiple images, and gives rise to glare, distorted and often poor vision. Its removal remains challenging, often requiring mechanical wiping or explantation. F_4H_5 is a new semifluorinated alkane into which silicone oil is readily soluble. The aim is to establish the effectiveness of F_4H_5 in removing silicone oil from three different types of IOL in vitro.

Method Silicone lenses (Tecnis ZM900, Advanced Medical Optics, Inc.), hydrophobic acrylic lenses (MA60, Alcon Laboratories, Inc.) and PMMA lenses (Ocular Vision, Inc) were first immersed in phosphate-buffered saline, second in silicone oil, then in F_4H_5 (Fluoron GmbH) for 10 min and lastly vigorously agitated in F_4H_5 for 1 min. They were weighed at each stage using scales accurate to 0.0001 g to measure the weight of the adherent oil. Dynamic contact angle (DCA) analysis was used to assess their surface properties.

Results Immersion in F_4H_5 alone removed 96.1% (±1.23) by weight of silicone oil from the hydrophobic acrylic lenses, 91.4% (±1.58) from the silicone and 95.6% (±1.44) from the PMMA IOLs. Immersion combined with 1 min of agitation increased the removal to 98.8% (±0.46) from the acrylic IOLs, to 93.7% (±0.48) from the silicone IOLs and to 100% (within ±0.0001 g) from every PMMA IOL. After treatment with F_4H_5, all IOL were optically clear. DCA hysteresis curves remained permanently altered. All measurements were highly reproducible.

Conclusion F_4H_5 was highly effective at removing the bulk of the silicone oil from all three groups of IOL. The DCA measurements suggested that their surface properties were permanently modified.

INTRODUCTION

Adherent silicone oil on intraocular lenses (IOL) following retinal detachment surgery induces large and irregular refractive errors and multiple images, and gives rise to glare, distorted and often poor vision.[1] The adherence is particularly tenacious to silicone lenses, but silicone oil has been shown to adhere to lenses made from other materials including PMMA and hydrophobic acrylic lenses.[2 3] Silicone oil usually comes into contact with the IOL when there is a breach in the posterior capsule. The adherence of the oil may, however, not be obvious until after oil removal. The oil droplets on the lenses have large contact angles, and they are dome-shaped, thus changing the refractive properties of the lenses.

Several methods have been advocated for dealing with adherent silicone oil droplets. In many cases, the method of last resort has been the explantation of the lenses.[4 5] Rinsing with sodium hyaluronate 1% Healon[6] and mechanical wiping with sponge intraocular instruments[7] have also been advocated. Their effectiveness is limited, and the manoeuvres are sometimes traumatic. A novel approach has been to use solvents. Recently, semifluorinated alkanes and their oligomers were introduced.[8 9] Perfluorohexyloctane (F_6H_8, Fluoron, Neu-Ulm, Germany) and OL62HV have been used as endotamponade.[9 10] By virtue of their ampiphilic properties, they are capable of dissolving silicone oil.[8] In the case of F_6H_8, up to 36% of its weight of silicone oil can be dissolved by the semifluorinated alkane. After an initial report with encouraging results at removing 1000 cS of silicone oil from IOL,[11] a subsequent paper showed F_6H_8 to be of limited effectiveness, requiring additional mechanical wiping to remove the adherent oil.[12] Most surgeons found it physically impossible to remove all silicone oil from the surface of IOL. As a silicone oil solvent, F_6H_8 was disappointing, despite its promising physical properties.

Recently, F_4H_5, a new semifluorinated alkane, has been investigated and shown to have a greater solubility for silicone oil (up to 100% of its weight).[13] In their study, Liang *et al* used microscopy to determine the extent of silicone oil removal from the IOLs. The purpose of this study was to investigate further whether this increased solubility translated as a more efficient means for removing silicone oil from IOLs. This was investigated by measuring the weight of oil attached to IOLs allowing detection of very small amounts of oil and using surface contact angle measurements to determine if residual oil could be detected on the IOL, even when the weight change was below the sensitivity of the balance.

METHOD

Three groups of three lenses were used: Tecnis ZM900 multifocal silicone lenses, Alcon MA60 (+22.5 dpt) acrylic lenses and Ocularvision (+22.5 dpt) PMMA lenses.

IOLs were weighed while suspended in a pot to protect the surface and attached oil drop.

Dynamic contact angle (DCA) measurements were made using the Wilhelmy plate method with phosphate-buffered saline (PBS) as the solvent. The lenses were attached to the clip by one haptic, and the other was carefully removed. An automated DCA surface-tensiometer was used (Cahn DCA-322 and software). The machine was programmed to run through a cycle advancing 4 mm before receding 4 mm.

The measurement protocol was as follows:

1. The IOL were first immersed in PBS for 10 min.
2. They were then weighed.

Table 1 Weight measurements (g) of the intraocular lenses (IOL) using electronic scales accurate to one-ten thousandth of a gram

	Acrylic IOL (Alcon)			PMMA IOL (Ocularvision)			Silicone IOL (Pharmacia)		
	IOL1	IOL2	IOL3	IOL1	IOL2	IOL3	IOL1	IOL2	IOL3
Reference (g)	0.0183	0.0182	0.0182	0.0255	0.0257	0.0254	0.0216	0.0217	0.0217
Oil (g)	0.0299	0.0290	0.0292	0.0358	0.0363	0.0358	0.0403	0.0406	0.0409
F_4H_5 (immerse) (g)	0.0189	0.0186	0.0185	0.0258	0.0262	0.0260	0.0230	0.0232	0.0237
F_4H_5 (shake) (g)	0.0185	0.0183	0.0183	0.0255	0.0257	0.0254	0.0228	0.0228	0.0230

3. Baseline contact angle measurements were carried out.
4. The lenses were then completely immersed in silicone oil (1000 cS).
5. The lenses were lifted out of the silicone oil and suspended in air so that excess silicone oil was allowed to drip off.
6. The lenses with the adherent silicone were weighed.
7. This was followed by the second contact-angle measurement.
8. The IOL were completely immersed in F_4H_5 for 10 min.
9. They were lifted out of the F_4H_5 and weighed for the third time.
10. Finally, all IOL were vigorously agitated in F_4H_5 for 1 min using a vortex mixer.
11. The lenses were lifted out of the F_4H_5 and weighed for the final time.
12. Final contact angle measurements were made. To avoid cross-contamination, fresh PBS, silicone oil and F_4H_5 were used with each set of experiments.

RESULTS

Lens weight measurements

The amount of silicone oil adherent to the IOL was calculated from the weight of the IOLs before and after immersion in the silicone oil. The greatest amount of silicone oil 18.9 (±0.03) mg was adherent to the silicone lenses, followed by the hydrophobic acrylic lenses with 11.1 (±0.04) mg and then PMMA lenses with 10.4 (±0.02) mg (table 1). These values of the additional weight after immersion in silicone oil were taken to be 100% of the amount of silicone oil adherent to the lenses. Adherent silicone oil was observed on all IOLs after immersion as shown in figure 1A.

Immersion in F_4H_5

Immersion in F_4H_5 alone removed 91.4 (±1.58)% by weight of silicone oil from the silicone lenses, 96.1 (±1.23)% from the hydrophobic acrylic lenses and 95.6 (±1.44)% from the PMMA lenses (table 1).

Agitation in F_4H_5

Immersion combined with 1 min of agitation in F_4H_5 increased the removal of silicone oil to 93.7% (±0.48) from silicone lenses, 98.8% (±0.46) from the hydrophobic acrylic lenses and 100% (within ±0.0001 g) from all PMMA lenses (table 1). After agitation in F_4H_5, all IOLs were optically clear, and no silicone oil was apparent (figure 1B)

DCA measurements

The DCA hysteresis curves of the force measured versus the distance as the IOL advanced (or withdrew) into the PBS were recorded for each IOL. Each hysteresis curve presented is an average of three curves. The curves start as the lens makes contact with the PBS. At this point, there is an increase in force as the PBS meniscus rises up the lens (figure 2A). As the lens advances into the PBS the force seemed to decrease. This is due to increasing buoyancy as more and more of the IOL is immersed. When the IOL is raised out of the PBS, the force is higher due to the PBS causing a dragging force on the IOL (figure 2B).

The baseline DCA measurements for each IOL type were highly reproducible but different from each other (figure 3A). The actual contact angle is dependent on the gradient of the tangent to the curve and the perimeter of the IOL at that point; it is, therefore, difficult to calculate specific values for the IOLs. Comparisons of the shape of the curves and how they change following contact with different environments, however, can be used to evaluate the change in the surface properties of the lenses. Following contact with silicone oil, DCA hysteresis graphs of all three groups of IOL were altered, compared with their baseline curves. After removal of the adherent oil with F_4H_5, the contact angle curves of the lenses did not return to baseline for each IOL type, suggesting a permanent alteration of the surface properties of the IOLs (figure 3B–D). After immersion in oil and cleaning with F_4H_5, the curves for the silicone lenses and the Alcon lens were very similar to their respective curves before cleaning in F_4H_5. The curve for the PMMA lenses after cleaning with F_4H_5, however, was similar for the advancing curve, but the receding part of the curve appeared to be more similar to the reference PMMA lens curve. These data fit with the weight loss data, suggesting that it is easier to remove the silicone oil from the PMMA lenses than the more hydrophobic acrylic and silicone lenses.

DISCUSSION

The complete removal of silicone oil adherent to IOLs is difficult. Silicone lenses are particularly prone to the adherence of silicone oil, and the general recommendation is to avoid the implantation of silicone IOL in patients with retinal detachment or even in those patients who might be at risk as such.[1] The interaction of silicone oil with silicone lenses can be explained by considering the interfacial energetic at the lens/oil/aqueous interface. It will be energetically favourable for the silicone oil to be in contact

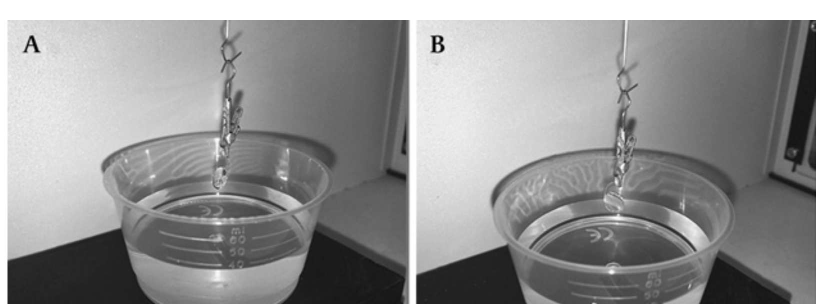

Figure 1 (A) Adherent silicone oil on the intraocular lenses (IOL). (B) After immersion in F_4H_5, the IOL is optically clear again.

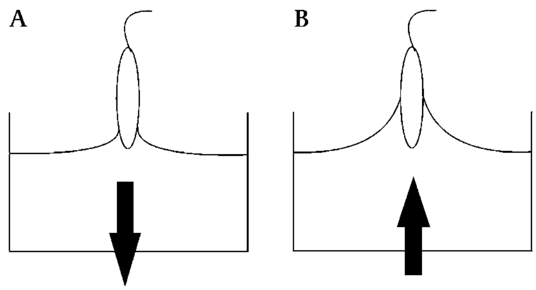

Figure 2 (A) As the lens advances into the PBS the force seemed to decrease due to increasing buoyancy as more and more of the intraocular lenses (IOL) is immersed. (B) When the IOL is raised out of the PBS the force is higher due to the PBS causing a dragging force on the IOL.

with the lens and exclude the aqueous owing to the hydrophobicity of the lens. In this study, it was demonstrated that there was more silicone oil adherent to silicone lenses (up to 181% more by weight) than PMMA IOL. Of the three lenses evaluated in this study, the PMMA lens would be expected to be the most hydrophilic, and thus the energetic driving force for the adherence of the silicone oil would be lowest. The hydrophobicity of the hydrophobic acrylic lenses would encourage silicone oil adherence, but it may not be as strong as to the silicone lenses. The DCA hysteresis curves support this explanation. The surface properties of the silicone and Alcon lenses after cleaning with F_4H_5 are the same as those after immersion in the oil for each lens type. The curves for the PMMA lenses after cleaning seem to be part way between those coated with oil and those before contact with the oil. Thus, it is suggested that the more hydrophilic the IOL, the easier it will be to remove the oil using F_4H_5.

F_6H_8 has been extensively studied by Langefeld *et al*.[11] The ease with which adherent oil droplet was removed depended on both the amount of silicone attached and the viscosity of the oil. It is known that the ability of a solvent to penetrate into a solute depends on the viscosity of the solute. Dick and Augustin also concluded that it might be beyond the ability of the F_6H_8 to dissolve it in amounts of oil larger than 2 μl.[14]

F_4H_5 has the ability to dissolve more silicone oil—up to 100% of its weight compared with 36% for F_6H_8. In a recent paper, Liang *et al* compared the use of the two agents at removing silicone oil adherent to lenses in vitro and in human in vivo experiments.[13] The in vitro experiments involve the removal of silicone droplets from a glass slide and silicone lenses. Their findings were recorded with microscopy and digital photography. The authors confirmed that F_4H_5 was effective and that F_6H_8 was not effective at removing silicone oil in different experimental settings. When used in 11 patients, they reported no significant postoperative inflammation in the vitreous cavity or in the anterior chamber associated with the use of F_4H_5.

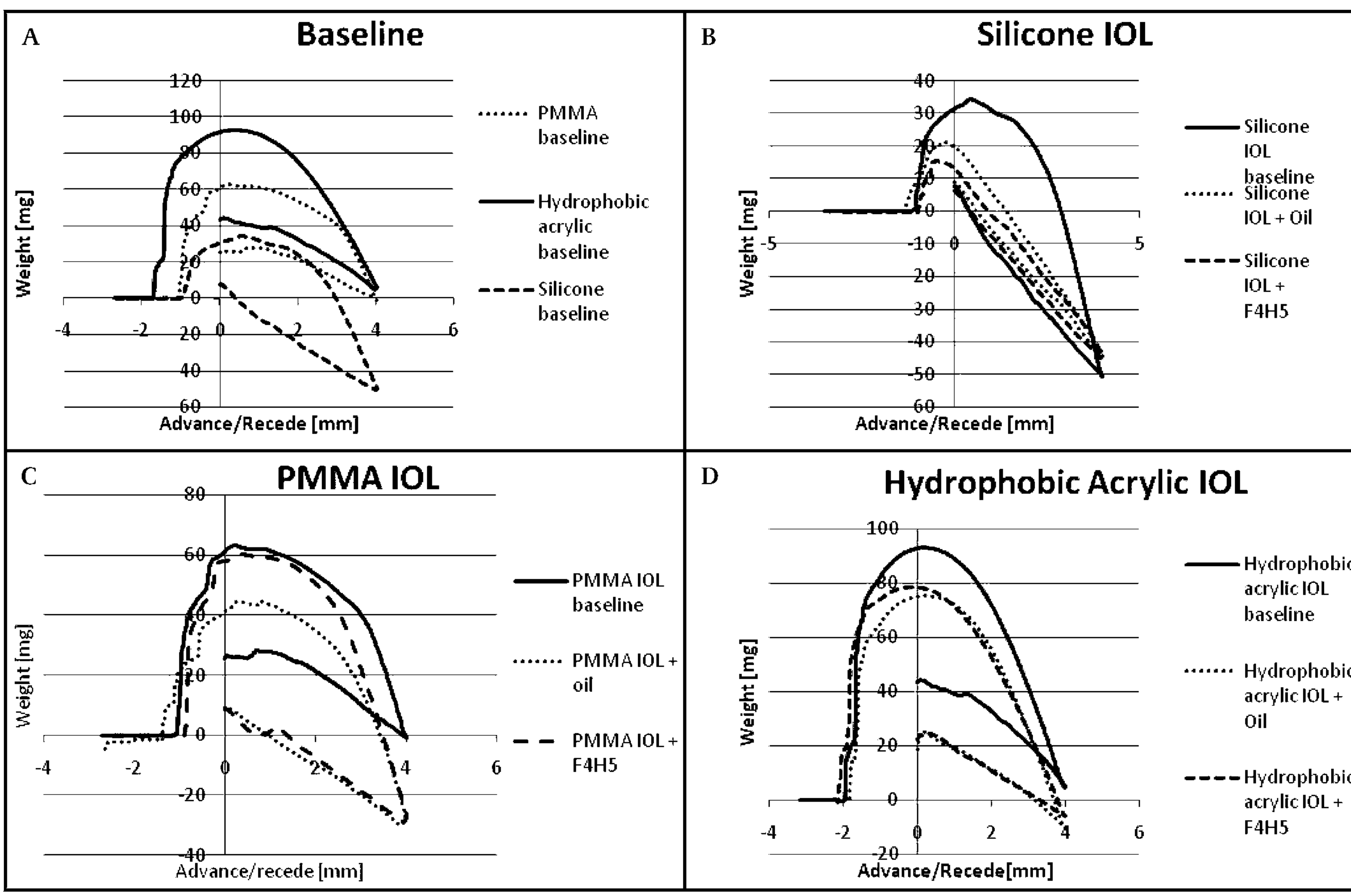

Figure 3 Representative DCA hysteresis curves. (A) Starting anticlockwise from the middle of the graph, each material shows a specific advancing curve (descending part of the curve) and receding curve (ascending part of the curve). The latter overshoots the initial point of contact due to prolonged adhesion of the PBS to the intraocular lenses (IOL) above the water line. Finally, a drop-off back to zero indicates the loss of contact between the PBS and the IOL. The baseline dynamic contact angle (DCA) measurements for each IOL type were highly reproducible (all three groups of IOL produced almost identical curves); however, each IOL type has a different-shaped hysteresis curve. (B—D) DCA hysteresis curves of all three groups of IOL (seen here as the average graphs of the three IOLs) were consistently altered compared with their baseline curves following immersion in silicone oil. After removal of the adherent oil with F_4H_5, the curves did not return to baseline, suggesting a permanent alteration of the surface properties of each IOL.

To study the efficiency of F_4H_5 at removing silicone oil, we used two very sensitive methods. First, using an electronic beam balance, we are able to detect changes in the weight of the IOL theoretically up to one-ten thousandth of a gram. We may therefore be able to detect residual oil or F_4H_5 adherent to the IOL, even when we may not be able to see droplets with the naked eye or with microscopy. Certainly, within the limit of our experiments (see below), we are confident that the F_4H_5 was able to remove the vast majority of silicone oil. In these experiments, an excess of F_4H_5 was used, and it is possible that longer immersion times could remove more of the oil.

Contact angle measurements are highly surface-sensitive and measure the surface properties of the outermost layer of the sample. Thus, even if the IOL was coated with a film of F_4H_5 or silicone oil no more than one molecule in thickness, the contact angle measurements will reflect the properties of this layer. Such a thin coating would again be too thin to be visible by the naked eye or by microscopy, and the total amount of oil will be too small to be detected by weighing the lenses. The fact that the contact angle hysteresis plot did not return to normal after F_4H_5 treatment indicated that the IOL had been permanently surface-modified. This irreversible change could be due to a very thin (invisible) coating of silicone, or alternatively, it could be due to a thin film of F_4H_5. We have no means of distinguishing between the two possibilities using our experiments.

These experiments had some limitations. The measurements of the weight of the IOL at baseline, after silicone oil, after F_4H_5 and after F_4H_5 with agitation were all done with the lenses 'wet'. At baseline, the IOL might have some PBS adherent to it, albeit not visible to the naked eye. This could theoretically be a source of error. Nonetheless, the results were highly reproducible (table 1). At the end of the whole cycle of experiments, the overall change in weight of the lenses (comparing baseline with final weight) was one hundredth of a gram or less. This attests to the efficiency of F_4H_5 at removing the bulk of the silicone oil.

In summary, this study has demonstrated that F_4H_5 is effective at removing the vast majority of the silicone oil from all groups of IOL. Our results confirm the findings of Liang *et al*[13] and concur with the results of earlier studies by Dick *et al*.[15] The salient point is that any changes in the surface properties may influence the biological compatibility of the lenses potentially altering their response to factors such as inflammation.

CONCLUSION

This study suggested that even though the majority of the oil could be removed by F_4H_5, the surface property of the lenses is permanently changed. This finding however is hopefully of no clinical significance in terms of the patient's vision, as all the lenses appeared optically clear with no adherent oil droplets, but the changed surface properties of the lens could lead to altered cellular responses.

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

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